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CLAIMS

- 1. A pharmaceutical composition for the treatment of depression, obsessive compulsive disorder and psychosis in a mammal, comprising: (a) a compound that exhibits activity, respectively, as an SRI antidepressant, or a pharmaceutically acceptable salt thereof; (b) atypical antipsychotic agent or pharmaceutically acceptable salt thereof; and (c) a pharmaceutically acceptable carrier; wherein the active agents "a" and "b" above are present in amounts that render the composition effective in treating, respectively, anxiety or depression, obsessive compulsive disorder and psychosis with improved efficacy.
- 2. A pharmaceutical composition according to claim 1, wherein the SRI or pharmaceutically acceptable salt thereof is selected from compounds of the formula I, and their pharmaceutically acceptable salts:

$$X_n$$
 A
 R^3
 R^1
 R^2
 R^4
 R^2

wherein phenyl ring A and phenyl ring B can each, independently, be replaced by a naphthyl group, and wherein when phenyl ring A is replaced by a naphthyl group, the ethereal oxygen of structure I and the carbon to which R³, R⁴ and NR¹R² are attached, are attached to adjacent ring carbon atoms of the naphthyl group and neither of said adjacent ring carbon atoms is also adjacent to a fused ring carbon atom of said naphthyl group;

n and m are, selected, independently, from one, two and three;

 R^1 and R^2 are selected, independently, from hydrogen (C_1 - C_4)alkyl, (C_2 - C_4)alkenyl, and (C_2 - C_4)alkynyl, or R^1 and R^2 , together with the nitrogen to which they are attached, form a four to eight membered saturated ring containing one or two heteroatoms, including the nitrogen to which R^1 and R^2 are attached, wherein the second heteroatom, when present, is selected from oxygen, nitrogen and sulfur, and wherein said ring may optionally be substituted at available binding sites with from one to three substituents selected, independently, from hydroxy and (C_1 - C_6)alkyl;

 R^3 and R^4 are selected, independently, from hydrogen and (C_1-C_4) alkyl optionally substituted with from one to three fluorine atoms, or R^3 and R^4 together with the carbon to which they are attached, form a four to eight membered saturated carbocyclic ring, and wherein said ring may optionally be substituted at available binding sites with from one to three substituents selected, independently, from hydroxy and (C_1-C_6) alkyl;

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or R^2 and R^3 , together with the nitrogen to which R^2 is attached and the carbon to which R^3 is attached, form a four to eight membered saturated ring containing one or two heteroatoms, including the nitrogen to which R^2 is attached, wherein the second heteroatom, when present, is selected from oxygen, nitrogen and sulfur, and wherein said ring may optionally be substituted at available binding sites with from one to three substituents selected, independently, from hydroxy and (C_1-C_6) alkyl;

each X and each Y is selected, independently, from hydrogen, halo (<u>i.e.</u>, chloro, fluoro, bromo or iodo), (C_1-C_4) alkyl optionally substituted with from one to three fluorine atoms, (C_1-C_4) alkoxy optionally substituted with from one to three fluorine atoms, cyano, nitro, amino, (C_1-C_4) alkylamino, di-[(C_1-C_4) alkyl]amino, NR⁵(C=O)((C_1-C_4) alkyl wherein R⁵ is hydrogen or (C_1-C_6) alkyl, and SO_p((C_1-C_6) alkyl wherein p is zero, one or two; and

with the proviso that: (a) no more than one of NR^1R^2 , CR^3R^4 and R^2NCR^3 can form a ring; and (b) at least one X must be other than hydrogen when (i) R^3 and R^4 are both hydrogen, (ii) R^1 and R^2 are selected, independently, from hydrogen and (C_1-C_4) alkyl, and (iii) ring B is mono- or disubstituted with, respectively, one or two halo groups;

or a pharmaceutically acceptable salt thereof.

- 3. A compound or salt according to claim 2, wherein n is one, X is fluoro, R^3 and R^4 are hydrogen, R^1 is hydrogen, R^2 is methyl, m is two and Y is Y_m is 3,4-dichloro.
- 4. A compound or salt according to claim 2, wherein m is zero, n is one, R³ and R⁴ are hydrogen, X is chloro, bromo, iodo or methyl, R¹ is hydrogen and R² is methyl.
- 5. A compound or salt according to claim 2, wherein said compound or salt is selected from the following compounds and their pharmaceutically acceptable salts:

[2-(3,4-Dichlorophenoxy)-5-fluorobenzyl]-dimethylamine;

[2-(3,4-Dichlorophenoxy)-5-fluorobenzyl]-methylamine;

25 [2-(3,4-Dichlorophenoxy)-5-trifluoromethylbenzyl]-dimethylamine;

N-[4-(3,4-Dichlorophenoxy)-3-dimethylaminomethylphenyl]-acetamide;

{1-[2-(3,4-Dichlorophenoxy)phenyl]-ethyl}-dimethylamine;

[2-(3,4-Dichlorophenoxy)-4-trifluoromethylbenzyl]-dimethylamine;

[2-(3,4-Dichlorophenoxy)-4-trifluoromethylbenzyl]-methylamine;

30 [4-Chloro-2-(3,4-dichlorophenoxy)-benzyl]-methylamine;

{1-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-ethyl}-methylamine;

{1-[2-(3,4-Dichlorophenoxy)phenyl}-ethyl}-methylamine;

{1-[2-(4-Chlorophenoxy)phenyl]ethyl}-methylamine;

[2-(3,4-Dichlorophenoxy)-5-methoxybenzyl]-methylamine;

35 [2-(4-Chlorophenoxy)-5-fluorobenzyl]-methylamine;

{1-[2-(4-Chlorophenoxy)-5-fluorophenyl]-ethyl}-methylamine;

[2-(3,4-Dichlorophenoxy)-5-methylbenzyl]-dimethylamine;

[4-Bromo-2-(3,4-dichlorophenoxy)-benzyl]-methylamine;

	[5-Bromo-2-(3,4-dichlorophenoxy)-benzyl]-methylamine;
	[2-(3,4-Dichlorophenoxy)-4,5-dimethoxybenzyl]-methylamine;
	[2-(3,4-Dichlorophenoxy)-4-methoxybenzyl]-dimethylamine;
	4-(3,4-Dichlorophenoxy)-3-methylaminomethyl-benzonitrile;
5	[2-(3,4-Dichlorophenoxy)-4,5-dimethylbenzyl]-methylamine;
•	3-(3,4-Dichlorphenoxy)-4-methylaminomethyl-benzonitrile;
	(+)-{1-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-ethyl}-methylamine;
	(-)-{1-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-ethyl}-methylamine;
	[2-(3,4-Dichlorophenoxy)-5-trifluoromethyl-benzyl]-methylamine;
10	[2-(3,4-Dichlorophenoxy)-4-methoxybenzyl]-methylamine;
10	[2-(4-Chloro-3-fluorophenoxy)-5-fluorobenzyl]-methylamine;
	[2-(3-Chloro-4-fluorophenoxy)-5-fluorobenzyl]-methylamine;
	(+/-)-2-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-pyrrolidine;
	(-)-2-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-pyrrolidine;
15	(+)-2-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-pyrrolidine;
	2-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-N-methylpyrrolidine;
	{1-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-1-methylethyl}-methylamine;
	{1-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-1-methylethyl}-dimethylamine;
	[4-Chloro-2-(4-chlorophenoxy)-5-fluorobenzyl]-methylamine;
20	[2-(3,4-Dichlorophenoxy)-5-fluoro-4-methoxybenzyl]-methylamine;
	[4-(3,4-Dichlorophenoxy)-3-(dimethylaminomethyl)-phenyl]-dimethylamine
	[5-Fluoro-2-(4-fluoro-3-methoxyphenoxy)-benzyl]-dimethylamine;
	[2-(4-Chlorophenoxy)-5-isopropylbenzyl]-methylamine;
	{1-[2-(4-Chlorophenoxy)-5-trifluoromethylphenyl]-ethyl}-methylamine;
25	[2-(4-Chlorophenoxy)-4,5-dimethylbenzyl]-methylamine;
	{1-[5-Chloro-2(3,4-dichlorophenoxy)phenyl]-propyl}-methylamine;
	[2-(3,4-Dichlorophenoxy)-5-methylsulfanyl-benzyl]-methylamine;
	{1-[2-(3,4-Dichlorophenoxy)-5-methylsulfanyl-phenyl]-ethyl}-methylamine;
	{1-[2-(3,4-Dichloro-phenoxy)-5-methylsulfanyl-phenyl]-1-methylethyl}-methylamine;
30	[2-(3,4-Dichlorophenoxy)-5-methylsulfanyl-benzyl]-dimethylamine;
	[2-(3,4-Dichlorophenoxy)-5-methanesulfinyl-benzyl]-dimethylamine;
	[2-(3,4-Dichlorophenoxy)-5-methanesulfinyl-benzyl]-methylamine;
	[2-(3,4-Dichlorophenoxy)-5-methanesulfonyl-benzyl]-methylamine;
	[2-(3,4-Dichlorophenoxy)-5-methanesulfonyl-benzyl]-dimethylamine;
35	[2-(3,4-Dichlorophenoxy)-5-(propane-2-sulfonyl)-benzyl]-methylamine;
	2-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-piperidine;
	2-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-1-methyl-piperidine;
	3-[2-(3,4-Dichlor-phenoxy)-5-fluorophenyl]-4-methyl-morpholine;

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2-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-1,2-dimethyl-piperidine;

{1-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-cyclopropyl}-dimethylamine;

2-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-1,5-dimethyl-pyrrolidine;

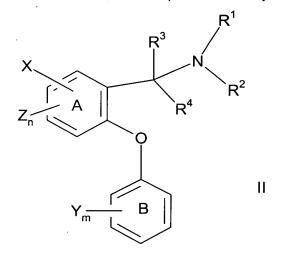
3-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-4-methyl-thiomorpholine;

{1-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-cyclopentyl}-methylamine;

{1-[2-(3,4-Dichlorophenoxy)-5-(propane-2-sulfonyl)-phenyl]-ethyl}-methylamine; and

[4-Chloro-2-(3,4-dichlorophenoxy)-5-methanesulfonyl-benzyl]-methylamine.

6. A pharmaceutical composition according to claim 1, wherein the SRIantidepressant agent or pharmaceutically acceptable salt thereof is selected from compounds of the formula II, as defined below, and their pharmaceutically acceptable salts:



wherein phenyl ring A and phenyl ring B can each, independently, be replaced by a naphthyl group, and wherein when phenyl ring A is replaced by a naphthyl group, the ethereal oxygen of formula II and the carbon to which R³, R⁴ and NR¹R² are attached, are attached to adjacent ring carbon atoms of the naphthyl group and neither of said adjacent ring carbon atoms is also adjacent to a fused ring carbon atom of said naphthyl group;

n and m are, selected, independently, from one, two and three:

 R^1 and R^2 are selected, independently, from hydrogen, (C_1-C_4) alkyl, (C_2-C_4) alkenyl, and (C_2-C_4) alkynyl, or R^1 and R^2 , together with the nitrogen to which they are attached, form a four to eight membered saturated ring containing one or two heteroatoms, including the nitrogen to which R^1 and R^2 are attached, wherein the second heteroatom, when present, is selected from oxygen, nitrogen and sulfur, and wherein said ring may optionally be substituted at available binding sites with from one to three substituents selected, independently, from hydroxy and (C_1-C_6) alkyl;

R³ and R⁴ are selected, independently, from hydrogen and (C₁-C₄) alkyl optionally substituted with from one to three fluorine atoms, or R³ and R⁴ together with the carbon to which they are attached, form a four to eight membered saturated carbocyclic ring, and

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wherein said ring may optionally be substituted at available binding sites with from one to three substituents selected, independently, from hydroxy and (C₁-C₆)alkyl;

or R^2 and R^3 , together with the nitrogen to which R^2 is attached and the carbon to which R^3 is attached, form a four to eight membered saturated ring containing one or two heteroatoms, including the nitrogen to which R^2 is attached, wherein the second heteroatom, when present, is selected from oxygen, nitrogen and sulfur, and wherein said ring may optionally be substituted at available binding sites with from one to three substituents selected, independently, from hydroxy and (C_1-C_6) alkyl;

each X is selected, independently, from phenyl, heteroaryl and heterocycle, and wherein each X may be further substituted by hydrogen, halo, (C_1-C_4) alkyl optionally substituted with from one to three fluorine atoms, (C_1-C_4) alkoxy optionally substituted with from one to three fluorine atoms, cyano, nitro, amino, hydroxy, carbonyl, (C_1-C_4) alkylamino, di- $[(C_1-C_4)$ alkyl]amino, NR⁵(C=O)(C₁-C₄)alkyl, SO₂NR⁵R⁶ and SO_p(C₁-C₆)alkyl, wherein R⁵ and R⁶ are selected, independently, from hydrogen and (C_1-C_6) alkyl, and p is zero, one or two;

each Y is selected, independently, from hydrogen, halo, (C_1-C_4) alkyl optionally substituted with from one to three fluorine atoms, (C_1-C_4) alkoxy optionally substituted with from one to three fluorine atoms, cyano, nitro, amino, (C_1-C_4) alkylamino, di-[(C_1-C_4) alkyl]amino, NR⁵(C=O)(C₁-C₄)alkyl, SO₂NR⁵R⁶ and SO_p(C₁-C₆)alkyl, wherein R⁵ and R⁶ are selected, independently, from hydrogen and (C_1-C_6) alkyl, and p is zero, one or two; and

each Z is selected independently from hydrogen, halo, (C_1-C_4) alkyl optionally substituted with from one to three fluorine atoms, (C_1-C_4) alkoxy;

or a pharmaceutically acceptable salt thereof.

- 7. A compound of salt according to claim 6, wherein ring B is phenyl, not replaced with a naphthyl group.
 - 8. A compound or salt according to claim 6, wherein each Y is hydrogen or halo.
- 9. A compound or salt according to claim 7, wherein m is 1 or 2, and wherein each Y is chlorine.
- 10. A compound or salt according to claim 6, wherein X is selected from furan, thiophene, pyrrole, and 1,2,3-triazole, and wherein X may be further substituted.
- 11. A compound or salt according to claim 6, wherein each Z is selected from hydrogen and halo.
 - 12. A compound or salt according to claim 11, wherein each Z is hydrogen.
- 13. A compound or salt according to claim 6, wherein R^3 and R^4 are independently selected from hydrogen and unsubstituted (C_1 - C_4) alkyl.
- 14. A compound or salt according to claim 13, wherein one or both of R³ and R⁴ are hydrogen.
 - 15. A compound or salt according to claim 6, wherein R^1 and R^2 are independently selected from hydrogen and unsubstituted (C_1 - C_4)alkyl.

- 16. A compound or salt according to claim 15, wherein one of R^1 and R^2 is hydrogen and the other of R^1 and R^2 is (C_1-C_4) alkyl.
- 17. A compound or salt according to claim 15, wherein one of R¹ and R² is hydrogen and the other of R¹ and R² is methyl.
- 5 18. A compound according to claim 6, selected from the group consisting of:
 - [4-(3,4-Dichlorophenoxy)-biphenyl-3-ylmethyl]-methylamine;
 - [2-(3,4-Dichlorophenoxy)-5-thiophen-3-ylbenzyl]-methylamine;
 - [2-(3,4-Dichlorophenoxy)-4-thiophen-3-ylbenzyl]-methylamine;
 - [2-(3,4-Dichlorophenoxy)-4-furan-2-ylbenzyl]-methylamine;
- 10 [2-(3,4-Dichlorophenoxy)-5-furan-2-ylbenzyl]-methylamine;
 - N-[4'-(3,4-Dichlorphenoxy)-3'-methylaminomethyl-biphenyl-3-yl]-acetamide;
 - [2-(3,4-Dichlorophenoxy)-5-thiophen-2-ylbenzyl]-methylamine;
 - [4-(3,4-Dichlorophenoxy)-4'-fluoro-biphenyl-3-ylmethyl]-methylamine;
 - [2-(3,4-Dichlorophenoxy)-5-[1,2,3]triazol-1-ylbenzyl]-methylamine;
- 15 [2-(3,4-Dichlorophenoxy)-5-[1,2,3]triazol-2-ylbenzyl]-methylamine;
 - [2-(3,4-Dichlorophenoxy)-5-pyridin-2-ylbenzyl]-methylamine;
 - [2-(3,4-Dichlorophenoxy)-5-pyridin-3-ylbenzyl]-methylamine;
 - 1-[4-(3,4-Dichlorophenoxy)-3-methylaminomethyl-phenyl]-1H-pyrazol-3-ylamine;
 - [2-(3,4-Dichlorophenoxy)-5-pyridin-4-ylbenzyl]-methylamine;
- 20 [3-(3,4-Dichlorophenoxy)-biphenyl-4-ylmethyl]-methylamine;
 - [4-(3,4-Dichlorophenoxy)-4'-methyl-biphenyl-3-ylmethyl]-methylamine;
 - [2-(3,4-Dichlorophenoxy)-4-thiophen-2-ylbenzyl]-methylamine;
 - [2-(3,4-Dichlorophenoxy)-5-pyrimidin-2-ylbenzyl]-methylamine;
 - [2-(3,4-Dichlorophenoxy)-5-pyrimidin-4-ylbenzyl]-methylamine;
- 25 [2-(3,4-Dichlorophenoxy)-5-(2-methylpyrimidin-4-yl)-benzyl]-methylamine;
 - {1-[2-(3,4-Dichlorophenoxy)-5-(2-methylpyrimidin-4-yl)-phenyl]-ethyl}-methylamine;
 - 4-[4-(3,4-Dichlorophenoxy)-3-(1-methylpyrrolidin-2-yl)-phenyl]-2-methylpyrimidine;
 - [2-(4-Chlorophenoxy)-5-(1-methyl-1H-pyrrol-3-yl)-benzyl]-dimethylamine;
 - [5-(1-methyl-1H-pyrrol-3-yl)-2-(naphthalen-2-yloxy)-benzyl]-dimethyl amine;
- 30 [5-Imidazol-1-yl-2-(naphthalen-2-yloxy)-benzyl]-dimethylamine;
 - 1,5,5-Trimethyl-3-[3-methylaminomethyl-4-(naphthalen-2-yloxy)-phenyl]-imidazolidine-2,4-dione;
 - 1-Methyl-3-[3-methylaminomethyl-4-(naphthalen-2-yloxy)-phenyl]-imidazolidine-2,4-dione;
- 35 3-[3-Methylaminomethyl-4-(naphthalen-2-yloxy)-phenyl]-thiazolidine-2,4-dione;
 - 3-[3-Methylaminomethyl-4-(naphthalen-2-yloxy)-phenyl]-oxazolidine-2,4-dione;
 - 3-[3-Methylaminomethyl-4-(naphthalen-2-yloxy)-phenyl]-oxazolidin-2-one;
 - 3-[3-Methylaminomethyl-4-(naphthalen-2-yloxy)-phenyl]-thiazolidin-2-one;

1-Methyl-3-[3-methylaminomethyl-4-(naphthalen-2-yloxy)-phenyl]-imidazolidin-2-one; 1-Methyl-3-[3-methylaminomethyl-4-(naphthalen-2-yloxy)-phenyl]-tetrahydro-pyrimidin-

2-one;

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1-[4-(3,4-Dichlorophenoxy)-3-methylaminomethyl-phenyl]-3-methyl-
 5
      tetrahydropyrimidin-2-one;
              1-[4-(3,4-Dichlorophenoxy)-3-methylaminomethyl-phenyl]-3-methylimidazolidin-2-one;
              3-[4-(3,4-Dichlorophenoxy)-3-methylaminomethyl-phenyl]-thiazolidin-2-one;
              3-[4-(3,4-Dichlorophenoxy)-3-methylaminomethyl-phenyl]-oxazolidin-2-one;
              [2-(3,4-Dichlorophenoxy)-5-(2-methylthiazol-4-yl)-benzyl]-methylamine;
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              [2-(3,4-Dichlorophenoxy)-5-(2-methyloxazol-4-yl)-benzyl]-methylamine;
              [2-(3,4-Dichlorophenoxy)-5-(2,5-dimethyloxazol-4-yl)-benzyl]-methylamine;
              [2-(3,4-Dichlorophenoxy)-5-(2,5-dimethylthiazol-4-yl)-benzyl]-methylamine;
              [2-(3,4-Dichlorophenoxy)-5-(5-methyl-[1,2,4]thiadiazol-3-yl)-benzyl]-methylamine;
              [2-(3,4-Dichlorophenoxy)-5-(5-methyl-[1,2,4]oxadiazol-3-yl)-benzyl]-methylamine;
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              [2-(3,4-Dichlorophenoxy)-5-[1,2,3]oxadiazol-4-yl-benzyl]-methylamine;
              [2-(3,4-Dichlorophenoxy)-5-(5-methyl-[1,2,3]thiadiazol-4-yl)-benzyl]-methylamine;
              [2-(3,4-Dichlorophenoxy)-5-(2,4-dimethyloxazol-5-yl)-benzyl]-methylamine;
              [2-(3,4-Dichlorophenoxy)-5-(2,4-dimethylthiazol-5-yl)-benzyl]-methylamine;
              [2-(3,4-Dichlorophenoxy)-5-[1,2,4]triazol-1-ylbenzyl]-methylamine;
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              [2-(3,4-Dichlorophenoxy)-5-(3-methyl-[1,2,4]triazol-1-yl)-benzyl]-methylamine;
              [2-(4-Chlorophenoxy)-5-(3,5-dimethyl-[1,2,4]triazol-1-yl)-benzyl]-methylamine;
              [2-(4-Chlorophenoxy)-5-tetrazol-1-ylbenzyl]-methylamine;
              [2-(4-Chlorophenoxy)-5-(5-methyltetrazol-1-yl)-benzyl]-dimethylamine;
              [2-(4-Chlorophenoxy)-5-[1,2,4]triazol-4-ylbenzyl]-dimethylamine;
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              [2-(4-Chlorophenoxy)-5-(1-methyl-1H-tetrazol-5-yl)-benzyl]-dimethylamine; and
              {1-[2-(3,4-Dichlorophenoxy)-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-ethyl}-
      dimethylamine.
                      A pharmaceutical composition according to claim 1 wherein the atypical
      antipsychotic agent or a pharmaceutically acceptable salt thereof is selected from:
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              abaperidone
              7-[3-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]propoxy]-3-(hydroxymethyl)-4H-1-
      benzopyran-4-one;
              belaperidone
              (1a,5a,6a)-3-[2-[6-(4-fluorophenyl)-3-azabicyclo[3.2.0]-hept-3-yl]ethyl]-
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8-chloro-11-(4-methyl-1-piperazinyl)-5H-dibenzo[b,e][1,4]diazepine

71. 126

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2,4(1H,3H)quinazolinedione; clozapine

iloperidone

olanzapine

1-[4-[3-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperdinyl]-3-methoxyphenyl]ethanone;

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2-methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2,3-b][1,5]benzodiazepine;
              perospirone
              cis-2-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]butyl]-hexahydro-1H-isoindole-
 5
      1,3(2H)-dione;
              risperidone
              3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)piperidino]ethyl]-2-methyl-6,7,8,9-tetrahydro-
      4H-pyrido[1,2-\alpha]pyrimidin-4-one;
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              sertindole
              1-[2-[4-[5-chloro-1-(4-fluorophenyl-1H-indol-3yl]-1-piperidinyl]ethyl]imidazolidin-2-one;
              tiospirone
              8-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]butyl]-8-azaspiro[4.5]decane-7,9-dione;
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              5-[2-[4-(1,2-benzisothiazole-3-yl)-1-piperazinyl]ethyl]-6-chloro-1,3-dihydro-2H-indol-2-
      one:
              zotepine
              2-[(8-chlorodibenzo[b,f]thiepin-10-yl)oxy]-N,N-dimethyl-ethanamine;
              quetiapine
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              5-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1piperazinyl)ethoxy]ethanol; and
              blonanserin
              2-(4-ethyl-1-piperazinyl)-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydro-
      cycloocta[b]pyridine.
          20 21
                      A pharmaceutical composition according to claim 1 wherein the amount of the
25
      SRIantidepressant, or pharmaceutically acceptable salt thereof, in said composition is from
      about 0.05 mg to about 1500 mg and the amount of the atypical antipsychotic agent or
      pharmaceutically acceptable salt thereof is from about 0.5 mg to about 1500 mg.
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A pharmaceutical composition according to claim 21 wherein the amount of the SRI antidepressant, or pharmaceutically acceptable salt thereof, in said composition is from about 2.5 mg to about 500 mg and the amount of the atypical antipsychotic or pharmaceutically acceptable salt thereof is from about 5 mg to about 200 mg.

A method of treating anxiety or depression, obsessive disorder, and psychosis in a mammal, comprising administering to said mammal: (a) a compound that exhibits activity as an SRI antidepressant, or a pharmaceutically acceptable salt thereof; and (b) atypical antipsychotic or pharmaceutically acceptable salt thereof; wherein the active agents "a" and "b" above are present in amounts that render the combination of the two agents effective in treating, respectively, anxiety or depression, obsessive compulsive disorder, and psychosis.

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The method according to claim 23, wherein the SRI antidepressant or pharmaceutically acceptable salt thereof is selected from compounds of the formula I,

$$X_n$$
 A
 R^3
 R^1
 R^2
 Y_m
 B

wherein phenyl ring A and phenyl ring B can each, independently, be replaced by a naphthyl group, and wherein when phenyl ring A is replaced by a naphthyl group, the ethereal oxygen of structure I and the carbon to which R³, R⁴ and NR¹R² are attached, are attached to adjacent ring carbon atoms of the naphthyl group and neither of said adjacent ring carbon atoms is also adjacent to a fused ring carbon atom of said naphthyl group;

n and m are, selected, independently, from one, two and three;

 R^1 and R^2 are selected, independently, from hydrogen (C_1 - C_4)alkyl, (C_2 - C_4)alkenyl, and (C_2 - C_4)alkynyl, or R^1 and R^2 , together with the nitrogen to which they are attached, form a four to eight membered saturated ring containing one or two heteroatoms, including the nitrogen to which R^1 and R^2 are attached, wherein the second heteroatom, when present, is selected from oxygen, nitrogen and sulfur, and wherein said ring may optionally be substituted at available binding sites with from one to three substituents selected, independently, from hydroxy and (C_1 - C_6)alkyl;

 R^3 and R^4 are selected, independently, from hydrogen and (C_1-C_4) alkyl optionally substituted with from one to three fluorine atoms, or R^3 and R^4 together with the carbon to which they are attached, form a four to eight membered saturated carbocyclic ring, and wherein said ring may optionally be substituted at available binding sites with from one to three substituents selected, independently, from hydroxy and (C_1-C_6) alkyl;

or R^2 and R^3 , together with the nitrogen to which R^2 is attached and the carbon to which R^3 is attached, form a four to eight membered saturated ring containing one or two heteroatoms, including the nitrogen to which R^2 is attached, wherein the second heteroatom, when present, is selected from oxygen, nitrogen and sulfur, and wherein said ring may optionally be substituted at available binding sites with from one to three substituents selected, independently, from hydroxy and (C_1-C_6) alkyl;

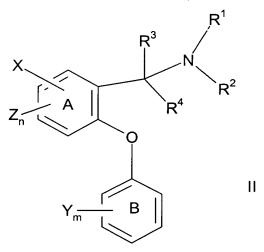
each X and each Y is selected, independently, from hydrogen, halo (<u>i.e.</u>, chloro, fluoro, bromo or iodo), (C_1-C_4) alkyl optionally substituted with from one to three fluorine atoms, (C_1-C_4) alkoxy optionally substituted with from one to three fluorine atoms, cyano, nitro, amino,

 (C_1-C_4) alkylamino, di-[(C_1-C_4) alkyl]amino, NR 5 (C=O)(C_1-C_4)alkyl wherein R 5 is hydrogen or (C_1-C_6) alkyl, and SO $_p$ (C $_1-C_6$)alkyl wherein p is zero, one or two; and

with the proviso that: (a) no more than one of NR^1R^2 , CR^3R^4 and R^2NCR^3 can form a ring; and (b) at least one X must be other than hydrogen when (i) R^3 and R^4 are both-hydrogen, (ii) R^1 and R^2 are selected, independently, from hydrogen and (C_1-C_4) alkyl, and (iii) ring B is mono- or disubstituted with, respectively, one or two halo groups;

or a pharmaceutically acceptable salt thereof.

The method according to claim 23, wherein the SRI antidepressant or pharmaceutically acceptable salt thereof is selected from compounds of the formula II,



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wherein phenyl ring A and phenyl ring B can each, independently, be replaced by a naphthyl group, and wherein when phenyl ring A is replaced by a naphthyl group, the ethereal oxygen of structure I and the carbon to which R³, R⁴ and NR¹R² are attached, are attached to adjacent ring carbon atoms of the naphthyl group and neither of said adjacent ring carbon atoms is also adjacent to a fused ring carbon atom of said naphthyl group;

n and m are, selected, independently, from one, two and three;

 R^1 and R^2 are selected, independently, from hydrogen, (C_1-C_4) alkyl, (C_2-C_4) alkenyl, and (C_2-C_4) alkynyl, or R^1 and R^2 , together with the nitrogen to which they are attached, form a four to eight membered saturated ring containing one or two heteroatoms, including the nitrogen to which R^1 and R^2 are attached, wherein the second heteroatom, when present, is selected from oxygen, nitrogen and sulfur, and wherein said ring may optionally be substituted at available binding sites with from one to three substituents selected, independently, from hydroxy and (C_1-C_6) alkyl;

R³ and R⁴ are selected, independently, from hydrogen and (C₁-C₄) alkyl optionally substituted with from one to three fluorine atoms, or R³ and R⁴, together with the carbon to which they are attached, form a four to eight membered saturated carbocyclic ring, and

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wherein said ring may optionally be substituted at available binding sites with from one to three substituents selected, independently, from hydroxy and (C₁-C₆)alkyl;

or R2 and R3, together with the nitrogen to which R2 is attached and the carbon to which R3 is attached, form a four to eight membered saturated ring containing one or two heteroatoms, including the nitrogen to which R2 is attached, wherein the second heteroatom, when present, is selected from oxygen, nitrogen and sulfur, and wherein said ring may optionally be substituted at available binding sites with from one to three substituents selected, independently, from hydroxy and (C₁-C₆)alkyl;

each X is selected, independently, from phenyl, heteroaryl and heterocycle, and wherein each X may be further substituted by hydrogen, halo, (C₁-C₄)alkyl optionally substituted with from one to three fluorine atoms, (C1-C4)alkoxy optionally substituted with from one to three fluorine atoms, cyano, nitro, amino, hydroxy, carbonyl, (C₁-C₄)alkylamino, di-[(C₁-C₄)alkyl]amino, NR⁵(C=O)(C₁-C₄)alkyl, SO₂NR⁵R⁶ and SO_p(C₁-C₆)alkyl, wherein R⁵ and R^6 are selected, independently, from hydrogen and (C_1-C_6) alkyl, and p is zero, one or two;

each Y is selected, independently, from hydrogen, halo, (C1-C4)alkyl optionally substituted with from one to three fluorine atoms, (C1-C4)alkoxy optionally substituted with from one to three fluorine atoms, cyano, nitro, amino, (C1-C4)alkylamino, di-[(C1-C₄)alkyl]amino, NR⁵(C=O)(C₁-C₄)alkyl, SO₂NR⁵R⁶ and SO₅(C₁-C₆)alkyl, wherein R⁵ and R⁶ are selected, independently, from hydrogen and (C₁-C₆)alkyl, and p is zero, one or two; and

each Z is selected independently from hydrogen, halo, (C1-C4)alkyl optionally substituted with from one to three fluorine atoms, (C₁-C₄)alkoxy;

or a pharmaceutically acceptable salt thereof. The method according to claim 23, wherein the SRI antidepressant, or pharmaceutically acceptable salt thereof, and the atypical antipsychotic agent or pharmaceutically acceptable salt thereof, are administered as part of the same dosage form.

26 27. The method according to claim 23, wherein the atypical antipsychotic agent, or pharmaceutically acceptable salt thereof, is administered in an amount from about 0.05 mg per day to about 1500 mg per day, and the antidepressant, or pharmaceutically acceptable salt thereof, is administered in an amount from about 0.05 mg day to about 1500 mg per day.

27 28. The method according to claim 23, wherein the atypical antipsychotic agent is administered in an amount ranging from about 5 mg per day to about 200 mg per day and the SRI antidepressant is administered in an amount ranging from about 2.5 mg per day to 500 mg per day.

28291 The method according to claim 23, wherein the atypical antipsychotic agent or pharmaceutically acceptable salt thereof is selected from:

abaperidone

7-[3-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]propoxy]-3-(hydroxymethyl)-4H-1benzopyran-4-one;

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belaperidone
              (1a,5a,6a)-3-[2-[6-(4-fluorophenyl)-3-azabicyclo[3.2.0]-hept-3-yl]ethyl]-
      2,4(1H,3H)quinazolinedione;
              clozapine
 5
              8-chloro-11-(4-methyl-1-piperazinyl)-5H-dibenzo[b,e][1,4]diazepine;
              iloperidone
              1-[4-[3-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperdinyl]-3-methoxyphenyl]ethanone;
              olanzapine
              2-methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2,3-b][1,5]benzodiazepine;
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              cis-2-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]butyl]-hexahydro-1H-isoindole-
      1,3(2H)-dione;
              risperidone
              3-[2-[4-(6-fluoro-1,2-benzaisoxazol-3-yl)piperidino]ethyl]-2-methyl-6,7,8,9-tetrahydro-
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      4H-pyrido[1,2-\alpha]pyrimidin-4-one;
              sertindole
              1-[2-[4-[5-chloro-1-(4-fluorophenyl-1H-indol-3yl]-1-piperidinyl]ethyl]imidazolidin-2-one;
              8-[4-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]butyl]-8-azaspiro[4.5]decane-7,9-dione;
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              ziprasidone
              5-[2-[4-(1,2-benzisothiazole-3-yl)-1-piperazinyl]ethyl]-6-chloro-1m3-dihydro-2H-indol-2-
      one;
              zotepine
              2-[(8-chlorodibenzo[b,f]thiepin-10-yl)oxy]-N,N-dimethyl-ethanamine;
25
              quetiapine
              5-[2-(4-dibenzo[b,f][1,4]thiazepin-17-yl-1piperaz-inyl)ethoxy]ethanol; and
              blonanserin
              2-(4-ethyl-1-piperazinyl)-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydro-
      cycloocta[b]pyridine.
        29 30.
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                      The method according to claim 25, wherein the SRI antidepressant agent or
      pharmaceutically acceptable salt thereof that is employed in such composition is selected
      from the following compounds and their pharmaceutically acceptable salts:
              [4-(3,4-Dichlorophenoxy)-biphenyl-3-ylmethyl]-methylamine;
              [2-(3,4-Dichlorophenoxy)-5-thiophen-3-ylbenzyl]-methylamine;
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[2-(3,4-Dichlorophenoxy)-4-thiophen-3-ylbenzyl]-methylamine; [2-(3,4-Dichlorophenoxy)-4-furan-2-ylbenzyl]-methylamine; [2-(3,4-Dichlorophenoxy)-5-furan-2-ylbenzyl]-methylamine;

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	N-[4'-(3,4-Dichlorphenoxy)-3'-methylaminomethyl-biphenyl-3-yl]-acetamide;
	[2-(3,4-Dichlorophenoxy)-5-thiophen-2-ylbenzyl]-methylamine;
	[4-(3,4-Dichlorophenoxy)-4'-fluoro-biphenyl-3-ylmethyl]-methylamine;
	[2-(3,4-Dichlorophenoxy)-5-[1,2,3]triazol-1-ylbenzyl]-methylamine;
	[2-(3,4-Dichlorophenoxy)-5-[1,2,3]triazol-2-ylbenzyl]-methylamine;
	[2-(3,4-Dichlorophenoxy)-5-pyridin-2-ylbenzyl]-methylamine;
	[2-(3,4-Dichlorophenoxy)-5-pyridin-3-ylbenzyl]-methylamine;
	1-[4-(3,4-Dichlorophenoxy)-3-methylaminomethylphenyl]-1H-pyrazol-3-ylamine;
	[2-(3,4-Dichlorophenoxy)-5-pyridin-4-ylbenzyl]-methylamine;
	[3-(3,4-Dichlorophenoxy)-biphenyl-4-ylmethyl]-methylamine;
	[4-(3,4-Dichlorophenoxy)-4'-methyl-biphenyl-3-ylmethyl]-methylamine;
	[2-(3,4-Dichlorophenoxy)-4-thiophen-2-ylbenzyl]-methylamine;
	[2-(3,4-Dichlorophenoxy)-5-pyrimidin-2-ylbenzyl]-methylamine;
	[2-(3,4-Dichlorophenoxy)-5-pyrimidin-4-ylbenzyl]-methylamine;
	[2-(3,4-Dichlorophenoxy)-5-(2-methylpyrimidin-4-yl)-benzyl]-methylamine;
	{1-[2-(3,4-Dichlorophenoxy)-5-(2-methylpyrimidin-4-yl)-phenyl]-ethyl}-methylamine;
	4-[4-(3,4-Dichlorophenoxy)-3-(1-methylpyrrolidin-2-yl)-phenyl]-2-methylpyrimidine;
	[2-(4-Chlorophenoxy)-5-(1-methyl-1H-pyrrol-3-yl)-benzyl]-dimethylamine;
	[5-(1-methyl-1H-pyrrol-3-yl)-2-(naphthalen-2-yloxy)-benzyl]-dimethyl amine;
	[5-Imidazol-1-yl-2-(naphthalen-2-yloxy)-benzyl]-dimethylamine;
	1,5,5-Trimethyl-3-[3-methylaminomethyl-4-(naphthalen-2-yloxy)-phenyl]-imidazolidine-
2,4-dio	ne;
	1-Methyl-3-[3-methylaminomethyl-4-(naphthalen-2-yloxy)-phenyl]-imidazolidine-2,4-
dione;	
	3-[3-Methylaminomethyl-4-(naphthalen-2-yloxy)-phenyl]-thiazolidine-2,4-dione;
	3-[3-Methylaminomethyl-4-(naphthalen-2-yloxy)-phenyl]-oxazolidine-2,4-dione;
	3-[3-Methylaminomethyl-4-(naphthalen-2-yloxy)-phenyl]-oxazolidin-2-one;
	3-[3-Methylaminomethyl-4-(naphthalen-2-yloxy)-phenyl]-thiazolidin-2-one;
	1-Methyl-3-[3-methylaminomethyl-4-(naphthalen-2-yloxy)-phenyl]-imidazolidin-2-one;
	1-Methyl-3-[3-methylaminomethyl-4-(naphthalen-2-yloxy)-phenyl]-tetrahydro-pyrimidin-
2-one;	
	1-[4-(3.4-Dichlorophenoxy)-3-methylaminomethyl-phenyl]-3-methyl-

1-[4-(3,4-Dichlorophenoxy)-3-methylaminomethyl-phenyl]-3-methyl-tetrahydropyrimidin-2-one;

1-[4-(3,4-Dichlorophenoxy)-3-methylaminomethyl-phenyl]-3-methylimidazolidin-2-one;

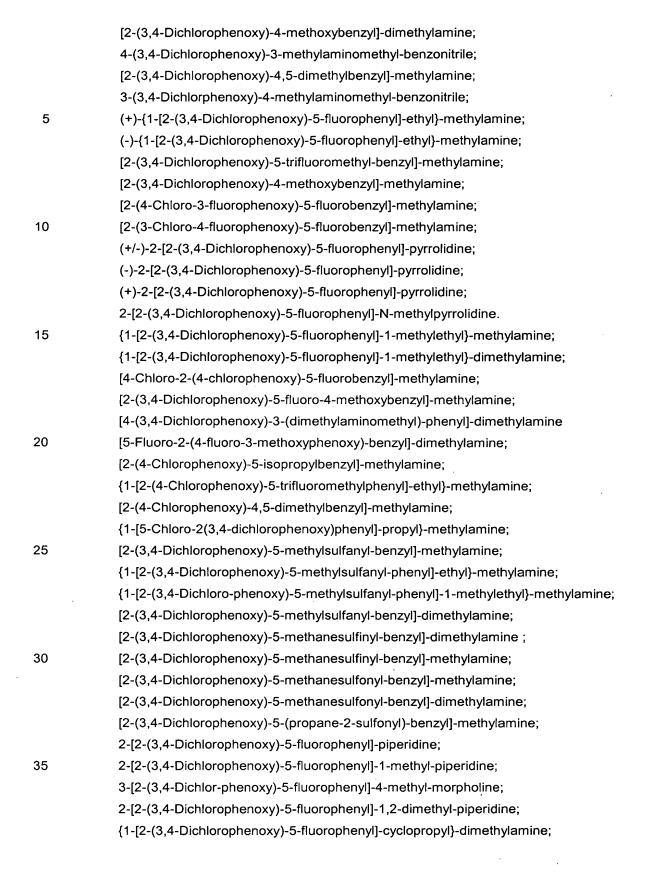
3-[4-(3,4-Dichlorophenoxy)-3-methylaminomethyl-phenyl]-thiazolidin-2-one;

3-[4-(3,4-Dichlorophenoxy)-3-methylaminomethyl-phenyl]-oxazolidin-2-one;

[2-(3,4-Dichlorophenoxy)-5-(2-methylthiazol-4-yl)-benzyl]-methylamine;

[2-(3,4-Dichlorophenoxy)-5-(2-methyloxazol-4-yl)-benzyl]-methylamine;

[2-(3,4-Dichlorophenoxy)-5-(2,5-dimethyloxazol-4-yl)-benzyl]-methylamine; [2-(3,4-Dichlorophenoxy)-5-(2,5-dimethylthiazol-4-yl)-benzyl]-methylamine; [2-(3,4-Dichlorophenoxy)-5-(5-methyl-[1,2,4]thiadiazol-3-yl)-benzyl]-methylamine; [2-(3,4-Dichlorophenoxy)-5-(5-methyl-[1,2,4]oxadiazol-3-yl)-benzyl]-methylamine; 5 [2-(3,4-Dichlorophenoxy)-5-[1,2,3]oxadiazol-4-yl-benzyl]-methylamine; [2-(3,4-Dichlorophenoxy)-5-(5-methyl-[1,2,3]thiadiazol-4-yl)-benzyl]-methylamine; [2-(3,4-Dichlorophenoxy)-5-(2,4-dimethyloxazol-5-yl)-benzyl]-methylamine; [2-(3,4-Dichlorophenoxy)-5-(2,4-dimethylthiazol-5-yl)-benzyl]-methylamine; [2-(3,4-Dichlorophenoxy)-5-[1,2,4]triazol-1-ylbenzyl]-methylamine; 10 [2-(3,4-Dichlorophenoxy)-5-(3-methyl-[1,2,4]triazol-1-yl)-benzyl]-methylamine; [2-(4-Chlorophenoxy)-5-(3,5-dimethyl-[1,2,4]triazol-1-yl)-benzyl]-methylamine; [2-(4-Chlorophenoxy)-5-tetrazol-1-ylbenzyl]-methylamine; [2-(4-Chlorophenoxy)-5-(5-methyltetrazol-1-yl)-benzyl]-dimethylamine; [2-(4-Chlorophenoxy)-5-[1,2,4]triazol-4-ylbenzyl]-dimethylamine; 15 [2-(4-Chlorophenoxy)-5-(1-methyl-1H-tetrazol-5-yl)-benzyl]-dimethylamine; and {1-[2-(3,4-Dichlorophenoxy)-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-ethyl}dimethylamine. 30 31. The method according to claim 24, wherein the antidepressant or pharmaceutically acceptable salt thereof that is employed in such method is selected from the 20 following compounds and their pharmaceutically acceptable salts: [2-(3,4-Dichlorophenoxy)-5-fluorobenzyl]-dimethylamine; [2-(3,4-Dichlorophenoxy)-5-fluorobenzyl]-methylamine; [2-(3,4-Dichlorophenoxy)-5-trifluoromethylbenzyl]-dimethylamine; N-[4-(3,4-Dichlorophenoxy)-3-dimethylaminomethylphenyl]-acetamide; 25 1-[2-(3,4-Dichlorophenoxy)phenyl]-ethyl}-dimethylamine; [2-(3,4-Dichlorophenoxy)-4-trifluoromethylbenzyl]-dimethylamine; [2-(3,4-Dichlorophenoxy)-4-trifluoromethylbenzyl]-methylamine; [4-Chloro-2-(3,4-dichlorophenoxy)-benzyl]-methylamine; {1-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-ethyl}-methylamine; 30 {1-[2-(3,4-Dichlorophenoxy)phenyl}-ethyl}-methylamine; {1-[2-(4-Chlorophenoxy)phenyl]ethyl}-methylamine; [2-(3,4-Dichlorophenoxy)-5-methoxybenzyl]-methylamine; [2-(4-Chlorophenoxy)-5-fluorobenzyl]-methylamine; {1-[2-(4-Chlorophenoxy)-5-fluorophenyl]-ethyl}-methylamine. 35 [2-(3,4-Dichlorophenoxy)-5-methylbenzyl]-dimethylamine; [4-Bromo-2-(3,4-dichlorophenoxy)-benzyl]-methylamine; [5-Bromo-2-(3,4-dichlorophenoxy)-benzyl]-methylamine; [2-(3,4-Dichlorophenoxy)-4,5-dimethoxybenzyl]-methylamine;



 $\hbox{2-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-1,5-dimethyl-pyrrolidine;}\\$

3-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-4-methyl-thiomorpholine;

 ${1-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-cyclopentyl}-methylamine;\\$

{1-[2-(3,4-Dichlorophenoxy)-5-(propane-2-sulfonyl)-phenyl]-ethyl}-methylamine; and

 $\label{prop:local_condition} \begin{picture}(4-Chloro-2-(3,4-dichlorophenoxy)-5-methane sulfonyl-benzyl]-methylamine. \end{picture}$